SURGICAL MANAGEMENT OF INSULIN OVERDOSE

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CASE REPORT

A middle-aged male was admitted to Accident and Emergency (A&E) claiming to have injected two full pens (600 IU) of insulin aspart (Novarapid®) and two full pens (600 IU) insulin glargine (Lantus®) into his anterior abdominal wall. He also claimed to have taken 14 tablets of temazepam 10mg. His past medical history included two previous overdose attempts, two myocardial infarctions, insulin dependent diabetes mellitus, hypertension, epilepsy and asthma. On examination, he was pale and sweaty with a heart rate of 100/min, blood pressure of 88/61mmHg and Glasgow Coma Scale of 15/15. His blood sugar, measured by BM-stix®, was 7.0 mmol/litre in the ambulance, 6.1 mmol/litre on arrival in A&E and 5.0 mmol/litre after receiving a bolus of 20% dextrose 500ml IV.

The maximum single injection of insulin aspart by Flexpen® is 60 IU and of insulin glargine by Optiset® is 40 IU. The claimed dose would thus have required at least 25 injections. In this patient, it was confirmed that all the insulin injection sites were within a circumscribed area, approximately 5cm diameter. Following discussion between the A&E, Intensive Care Unit (ICU), surgical and medical teams it was decided that surgical excision of the subcutaneous fat containing the injections site was the logical course of action and he was taken to the operating theatre. He remained hypoglycaemic through the peri-operative period despite being on an infusion of 50% dextrose (see table) and he was subsequently admitted to the High Dependency Unit (HDU). He started to eat and drink six hours after surgery and his blood sugar started to rise. His IV infusion was changed to 5% dextrose and he was transferred to a medical ward where his blood sugar remained high and he was started on his regular insulin dosage. Following a psychiatric assessment the next day, the patient was discharged from the hospital.

TIME	BLOOD SUGAR Mmo/litre BM Stix®
21:00 (Ambulance)	7.0
21:25 (A&E arrival)	6.1
21:45 (A&E dextrose)	5.0
01:25 (Recovery)	1.3
02:15	3.4
07:30	10.7
08:30	10.8
09:30	12.0
12:00	10.2
14:00	9.4
16:30	10.4
22:00	17.0

Table Blood sugar values recorded

DISCUSSION

Insulin overdose is potentially a fatal condition with hypoglycaemia as its chief presentation.⁽¹⁾ Symptoms include gastrointestinal, cardiovascular, central nervous system and electrolyte disturbances, eg hypokalaemia, hypophosphataemia and hypomagnesaemia.^(1,2,3,4) The speed of onset and the duration of the symptoms are related to the type of insulin and its route of administration.

The guidelines issued by the Guy's and St Thomas' Hospitals Poisons Unit suggest the following:⁽²⁾

1. Patient observations depending on the duration of action of insulin
2. Blood sugar measurements 15-30 min initially followed by hourly thereafter with lab checks twice a day
3. Monitor electrolytes – potassium, magnesium and phosphorus
4. Watch out for arrhythmias and cerebral oedema
5. Oral glucose as a first aid measure
6. Dextrose infusion – concentration and rate depends on blood sugar values. Cessation of therapy should be followed by at least two blood sugar values >6 mmol/l over an eight hour period
7. Glucagon – recommended when IV access/dextrose not available. Requires hepatic glycogen reserve for its action and this is quickly depleted in insulin overdose. Often does not work, and causes vomiting as its side effect. Use of glucagon should always be followed by dextrose therapy. Dose – 1mg IM, SC or rapid IV bolus
8. Surgery – as previously discussed
9. Interactions: beta-blockers will mask the symptoms of hypoglycaemia and may also potentiate it; ethanol may mask and delay the onset of hypoglycaemia; monoamine oxidase inhibitors (MAOIs), non-selective beta-blockers, angiotensin converting enzyme (ACE) inhibitors and anabolic steroids enhance hypoglycaemic effect; oral contraceptives, thyroid hormones, thiazides, sympathomimetics and corticosteroids increase insulin requirements

Insulin aspart is a rapid-acting insulin analogue. The onset of action occurs within 10-20 minutes of injection. Its maximum effect is exerted between one and three hours after the injection and its duration of action is three to five hours.

Insulin glargine is a long-acting recombinant human insulin analogue and is given once a day at bedtime. Lantus® consists of insulin glargine dissolved in a clear aqueous fluid. Each ml contains 100 IU (3.6378mg) insulin glargine, 30mcg zinc, 2.7mg m-cresol, 20mg glycerol 85% and water for injection. The pH is adjusted to approximately 4 by addition of aqueous solutions of hydrochloric acid and sodium hydroxide. Unlike other insulins it forms a local precipitate after subcutaneous injection, and insulin dimers and monomers are then released slowly into the circulation. Four hours after injection it reaches a plateau plasma level, which is maintained for at least 24 hours. After subcutaneous injection of 0.3 IU/Kg and 0.4 IU/Kg of insulin glargine,

metabolic activity returns to baseline values after 24 and 30 hours respectively.⁽³⁾

This patient had injected himself with approximately 6 IU/Kg of insulin aspart and insulin glargine, which could have taken several days of HDU stay with its attendant morbidity, prolonged infusions of hypertonic dextrose with its associated complications such as deranged liver functions,⁽⁴⁾ cerebral oedema, electrolyte disturbances and the need for a central line (for infusing hypertonic dextrose solution) with its associated complications. Managing this medical emergency surgically minimised the above issues. However, this patient was an anaesthetic challenge with his co-morbidities.

Surgical excision was recommended in a study in 1982.⁽⁵⁾ In 1993, another study recommended considering surgical excision where the injection is less than three hours earlier and the injection dose is massive and/or with a long-acting insulin injection.⁽⁶⁾ It should also be added that this is only practical if the overdose has been administered in a confined area.

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